Early Peyote Research
An Interdisciplinary Study[1]

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INTRODUCTION

> "Es apasionante el tema de la botánica medicinal en México. En cualquier parte del mundo la historia y la leyenda se mezclan en los relatos de las virtudes de algunas plantas, pero en el caso de México, la realidad apoya a la fantasía y la estricta relación histórica tiene un sabor de novela de aventuras.
>
> Efrén C. del Pozo

Peyote, the cactus *Lophophora williamsii*, has been called the prototype of the New World hallucinogens. First introduced to the scientific world in the 1880's, this Mexican plant, and the drug derived from it, "mescal buttons", are now well known from many points of view. From 1887 to the present, the bibliography on peyote has grown to enormous proportions.

In recent years extensive studies have covered various aspects of this plant, including the taxonomy and distribution of the genus *Lophophora* (Bravo, 1967; Anderson, 1969), the anthropology of the peyote cult (La Barre, 1964; Furst, 1972), the chemistry and biological effects of peyote constituents (Kapadia and Fayez, 1970, 1973; Shulgin, 1973), and the biosynthesis of peyote alkaloids (Lundström, 1971a; Paul, 1973).

The aim of the present paper is to present the early history of peyote research from 1887 to the turn of the century. We have tried to correlate the early findings with recent knowledge of the botany and chemistry of peyote, and in addition performed a phytochemical examination of an 85-year-old sample of "mescal buttons". Furthermore, the alkaloid contents of this old material and fresh material of *Lophophora williamsii* and *Lophophora diffusa* have been compared. As will become evident from the paper, the alkaloid analysis of *Lophophora diffusa* provides an explanation of several controversial and much discussed points in older research work.

EARLY PEYOTE RESEARCH

Although the use of peyote was noted very early by the Spanish conquerors of Mexico, their reports did not attract great attention, and peyote remained obscure until the 19th century. The first botanical studies

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[1] Cactaceae Alkaloids XIX. Part XVII, Econ. Bot. 27: 241 (1973). Part XVIII, J. Pharm. Sci. 63: 574 (1974). Submitted for publication July, 1974.

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appeared in the 1840's and the plant was also given a place in the Mexican Pharmacopoeia of 1846. For a compilation of the early sources, the reader is referred to Slotkin (1955) [4].

The spark that was to ignite the "peyote boom" was not lit until 1887 when Briggs published the first study of the effects of "muscale buttons". The pre-1900 peyote research that was to follow can be divided into two chapters, the first describing the events leading to the identification of the drug, the finding of pharmacologically active alkaloids, and the introduction of the drug into medical practice. This chapter is called "The Parke, Davis & Company story", in the following section.

The second chapter covers the further chemical investigations, the controversy over botanical names, and the studies of isolated alkaloids. We have called this chapter "The *Anhalonium lewinii* controversy".

The Parke, Davis & Company Story

Early peyote research is closely connected with the name of Louis Lewin. However, he was not the discoverer of the drug. Credit for having brought peyote to the attention of the medical world of the 1880's must go to Dr. John Raleigh Briggs of Dallas, Texas. An instrumental role was also played by the pharmaceutical manufacturers Parke, Davis & Company of Detroit.

Although Lewin (1888a) made reference to Parke, Davis & Co. as suppliers of his drug material, the company's "rough and ready" search for peyote was largely unknown until Bender (1968) reconstructed this fascinating story [5], and almost nothing was known about Briggs.

John Raleigh Briggs (1851-1907) was born in Tennessee, where he studied at the Nashville Medical College in 1873. In 1880 he graduated from the

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[4] Recently we have come across an early reference to peyote in Bartlett's "Dictionary of Americanisms" (third edition, published in 1860). Since this reference is not listed by Slotkin, we give it in full here:

> WHISKEY-ROOT. A plant of the Cactus species possessing intoxicating properties, which is thus described by a correspondent of the New Orleans Picayune: "It is what the Indians call Pie-o-ke. It grows in southern Texas, on the range of sand-hills bordering on the Rio Grande, and in gravelly, sandy soil. The Indians eat it for its exhilarating effect on the system, it producing precisely the same as alcoholic drinks. It is sliced as you would a cucumber, and these small pieces chewed, the juice swallowed, and in about the same time as comfortably tight cocktails would 'stir the divinity within' you, this indicates itself; only its effects are what I might term a little more *k-a-v-o-r-t-i-n-g*, giving rather a wilder scope to the imagination and actions."

This very early reference to peyote in the English language was cited by the English explorer Sir Richard Burton in his book "The Look of the West, 1860 — Across the Plains to California" (Burton, 1963, originally published in London, 1862). Interestingly, Burton compared the use of the "whiskey-root" with that of "the intoxicating mushroom of Siberia". This must be the earliest published comparison of these two hallucinogens. In the same year that Burton wrote his book, 1862, the uses and effects of the Siberian mushroom (the fly agaric, *Amanita muscaria*) had been described by M. C. Cooke in his "A Plain and Easy Account of British Fungi", the earliest popular manual on mushrooms in the English language (Wasson and Wasson, 1957). Also in 1862, Lewis Carroll created "Alice's Adventures in Wonderland" (first published in 1865). Wasson and Wasson (1957) think that the mushroom episode in Carroll's book was inspired by Cooke. It is probable that Cooke's manual was also Burton's source of mushroom information.

[5] Bender made extensive use of unpublished material, mainly letters received by Parke-Davis. Through the courtesy of Bender, it has been possible for us to study this unique material, and we will in the following supplement it with an equally unique material from Louis Lewin's own files. This Lewin material is now in the collection of one of us (B. H.). With regard to the Parke-Davis material, we have tried to avoid citing those letters already cited by Bender (1968).

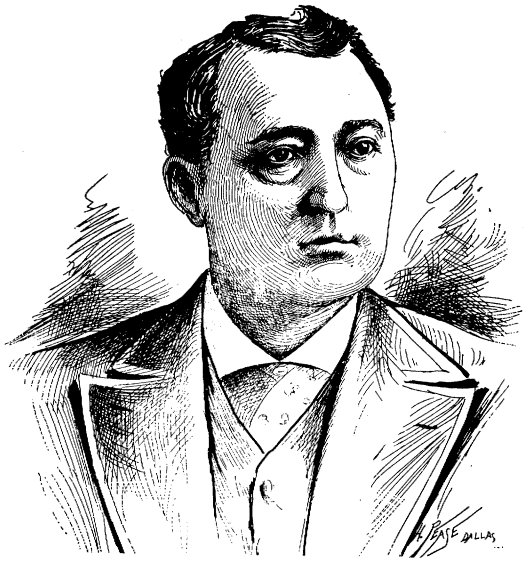

Fig. 1. John Raleigh Briggs (1851-1907).

Missouri Medical College in St. Louis and specialized in diseases of the eye, ear, nose and throat. He came to Dallas in 1882. He established and was the editor for many years of the *Texas Health Journal.* He also founded the Texas Private Sanatorium at Oak Bluff for the treatment of tuberculosis in 1889. In 1894 he went to Europe on a trip that included visits to Edinburgh, London and Paris. He was a member of the city council of Dallas and served two terms as its president (Giles, 1951).

Briggs fought in his journal and elsewhere against quackery, water pollution and city filth. It was his belief that a physician should advertise to compete with the quacks and to show the sick people that he had a service to offer them.

As an editor, Briggs was "an outspoken nonconformist who wrote what he thought and who kept a gun on his desk and a lawyer on his staff to support his views" (Baird, 1972). An 1892 biographer commented: "He is a writer of fine perceptions, with a polished style and finish worthy of one making greater literary claims". His writing ability twice earned him 100 dollars in gold for the best essay on a medical subject (Anonymous, 1892, p. 497).

On April 9th, 1887, there appeared in the *Medical Register* an article by Dr. Briggs describing his personal experience with a drug known to him only as "muscale buttons".[6] He reported as follows:

[6] "Muscale buttons" was an early misnomer for "mescal buttons". This type of distortion of Mexican words in American English is apparently not uncommon. In an early "Dictionary of Americanisms" we have found the following examples: *muskeet* for the Spanish *mezquite*; *mustang* for *mesteño*; and *mustee* for *mestizo* (Bartlett, 1860). "Mescal buttons" is also a misnomer, since "mescal" is derived from the Mexican "mezcal", which is the name of a distilled liquor obtained from the century plant (*Agave* sp.). The common confusion of the intoxicating peyote with alcoholic drinks (cf. footnote 4) is understandable but most unfortunate, and many attempts have been made to clarify this point (Schultes, 1937b).

I am wholly unfamiliar with the literature (if there be any) on this peculiar fruit. Learning *first* from my brother, who has spent several years among the different tribes of wild Indians, and subsequently from Mexicans, that both Indians and Mexicans eat (or chew and swallow the juice) this fruit for purposes of intoxication, I became interested in its physiological effects. The Indians use it that they may forget their troubles and see "beautiful visions"; such as "*buffalo and wild horses come up out of the earth*" (?).

In order to learn more of this curious fruit I sent to and procured from Mexico some specimens. The "buttons" are, while green, about two inches in diameter by one half in thickness, and are covered over with minute thistles, resembling very much several species of cactus. In fact that this is of the cactus family I feel confident. So far as I am aware it is indigenous to Mexico only, and is very valuable, being sent from there to the various tribes of wild Indians throughout the Southwest and sold for a high price. It is regarded by the Indians as a *sacred* plant, and is eaten only by the "medicine men," the chiefs, and other notable worthies. I have never seen those Indians under its influence, but have learned from reliable sources the following: An Indian will eat from six to ten (?) of those "buttons," after properly arranging himself in his "tepee," as does the opium smoker.

In a short time — two to four hours — he becomes totally unconscious, in which condition he remains for two or three days. After returning to consciousness he will relate to the natives many remarkable adventures in the "spirit world," and the return to the prairies of innumerable herds of buffalo and wild horses. The state of the pulse or rate of respiration was not ascertained, but I am informed they have all the appearances of opium poisoning. The "charm" over, the tribe cluster around to drink in the superstitious recitals of those savage leaders. Such hallucinations are to those superstitious Indians undoubted realities, and are a part of their religious creed. In giving my *personal experiences* I hope my motives will not be misconstrued. On being cut open while green those "buttons" emit a very disagreeable and pungent odor. The color of the cut surfaces is a brilliant green. The fruit is spongy, has a velvety touch, and is quite juicy.

Briggs himself took one-third of a "button" and concluded:

Whatever may be the ultimate constituents of this poison, it certainly is the most *violent* and *rapid* of all fruits, or even medicines, known to me — manifesting its first effects in less than fifteen minutes. I know of nothing like it except opium and cocaine. The most notable point is the rapidity with which it increases the heart's action. Next, the intoxication and subsequent depression. I think it well worth the trouble to investigate the matter. One man's experience is worth but little, and it is to be hoped some enterprising experimenter will carry out the research. As to *myself*, I must admit I feel somewhat abstemious on the subject.

Briggs' not too scientific article[7] was reprinted only a month later, in May 1887, in *The Druggists' Bulletin*. This time the article was seen by George S. Davis, Secretary and General Manager of Parke, Davis & Co. In a brief note of May 19th, 1887, Mr. Davis requested that Dr. Briggs be written to and enquiries made for more facts (Bender, 1968).

[7] Slotkin (1955) has commented that Briggs' hearsay account of the Indian use of the "buttons" is an "exasperating mixture of fact and fancy, but I do not know how to separate the two". It has also been questioned, whether the "muscale buttons" that produced so drastic effects in Dr. Briggs, did not derive from another species of cactus than *Lophophora williamsii*, since the effects of peyote were later found to be quite different (Prentiss and Morgan, 1895; Rouhier, 1927, p. 225).

Figs. 2 & 3. "Muscale Button." Top view (left) and bottom view (right) of a specimen sent by Rusby to Watson in July, 1887. (See *Experimental*: Plant Material.) Scale in centimeters.

The following letter from Dr. Briggs brought some of the desired information:

Office of THE TEXAS COURIER-RECORD OF MEDICINE
J. R. BRIGGS, M.D., Associate Editor

Dallas, Texas
May 24th 1887

Parke, Davis & Co.
DETROIT, Mich.

Gentlemen:

Yours of 20th inst. addressed to me at "Fort Worth(s)" relative to "Muscale buttons" just received. Replying to same will say the Muscale button does not grow in Texas but in old Mexico. I know but little of this, to me, very strange plant. During my residence in Texas for several years I have heard of this plant and only succeeded just in getting hold of it. The specimen I got was smuggled through from Mexico to Texas by a half breed Mexican who makes it a business to furnish the wild tribes of Indians with it; going annually (in the fall) and laying in a supply. The only way I know of for you to get the plant is through this same man whose address I do not at present know, but will ascertain

and write you. It is, I learn, used in Mexico for criminal purposes — "*making people crazy*" and subsequently putting them to "sleep", I came near to losing my life by eating a piece of one. There is so far as I can ascertain *absolutely* no literature in English on this plant. The profession in Mexico knows nothing of it so far as I can ascertain. I should not think you would want large quantities of it — "by the bale". I am certain 2 buttons would kill a *white* man. I have been for years and am yet much interested in this plant and will try to procure some more and experiment with it.

Any service I can render you I do with pleasure.

Respectfully yours,

J. R. Briggs, M.D.
723 Elm Str.

Information was also solicited from Dr. Henry H. Rusby, Professor of Botany, Physiology, and Material Medica at the College of Pharmacy of the City of New York, who served as a botanical consultant to Parke-Davis (Bender, 1968). In a letter to Mr. H. A. Wetzel, Superintendent at Parke, Davis & Co., Dr. Rusby reported that he had never heard of "muscale buttons". He commented that "Your correspondent's account of their action reminds me of the effects of the seeds of some species of *Sophora* . . . ."[8]

In Dallas, Dr. Briggs was now trying to obtain a supply of "buttons" for Parke-Davis. On June 8th he sent a cigar-box full of the "buttons" to Detroit (Bender, 1968).

Samples of this first shipment of "muscale buttons" were now distributed to various investigators. Thus, "buttons" were sent to Dr. Rusby, who was "entirely baffled", to use his own words in a letter to Mr. Wetzel of July, 1st. On July 9th, 1887, he forwarded some of the still unidentified "buttons" to Professor Sereno Watson of the Herbarium of Harvard University for botanical study [9] (Figs. 2 & 3). Already Briggs (1887) had expressed his opinion that the drug was derived from the cactus family, but this information was not discussed by Rusby, who instead told Watson that "the parties wish to make it proprietary, so our efforts to obtain and publish knowledge concerning it are opposed".

After careful study, Watson concluded (July 19th):

> The plant is cactaceous and I have no doubt should be referred to the genus *Anhalonium*, of which five species are known in Mexico. This, however, does not accord with any description that I find and may be a new one.

Samples of the new drug, or information about it, had also been sent to Dr. Louis Lewin in Germany. This is evident from a post-card, dated Berlin, July 3rd, 1887:

> Ich habe jetzt alles erhalten, und *will die Untersuchung übernehmen.* Sie können sich davon soviel als notwendig besorgen. Ich nechme mit Ihnen Rücksprache.
>
> Es grüsst bestens
>
> L. Lewin

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[8] For a discussion of *Sophora* seeds as a hallucinogen, sometimes in combination with peyote, and the role of these seeds in the peyote ceremony of the Kiowa Indians, the reader is referred to Schultes (1937a; 1972b).

[9] The "buttons" received by Watson are still in the collection of the Gray Herbarium of Harvard University. A part of this material has now been studied by us (see *Experimental*: Plant Material and *Results and Discussion*: The old Rusby Material).

Added on this card is the notation "Muscale Buttons" in the handwriting of Mr. Wetzel, the Superintendent.

July, 1887, was certainly not a time for holidays at Parke-Davis. In the analytical department, Frank Augustus Thompson, a member of the American Pharmaceutical Association, prepared alcoholic extracts of the new drug. His report to Mr. Wetzel, dated July 5th, 1887, is of special interest. In it he describes his finding that the drug "contains a large amount of alkaloid or rather alkaloids and I am quite certain that there is more than one".

After considerable difficulty, Briggs reported on July 17th that five bushels of "buttons" were on their way to Detroit (Bender, 1968). Information was also received from an illiterate Mexican who said that the "buttons" were called pellote[10] in Mexico. The following remarks were made by Rusby in a letter of July 26th:

> I note your suggestion that the name of muscale buttons should be changed to pellote, which I think a good one. As to calling the effect of the drug "pellotism", I must think about it . . . .

Fig. 4. Louis Lewin (1850-1929). Picture taken about the time of his trip to the United States.

Let us for a moment leave the summer heat of Detroit and focus our attention on Louis Lewin, the German pharmacologist who had also received samples of "muscale buttons".

Louis Lewin (1850-1929) was born in Western Prussia. He came to Berlin in 1854 and remained there almost all his life. He received his M.D. in 1875 at the University of Berlin, and in 1881 he became "Privatdozent" in

[10] In Spanish the "ll" sound is pronounced as an "y". Pellote and peyote are thus pronounced similarly, but this was not realized by the early American and German research workers (cf. footnote 16).

pharmacology. In 1894 he was named titular professor at the University of Berlin and established a private laboratory and lecture hall in Berlin (Holmstedt, 1967).

Lewin was an extraordinary lecturer and an enthusiastic research worker. From 1874 to 1929 he published 248 major publications. Most of his time was devoted to the side effects of drugs, but he also wrote a toxicology textbook, a comprehensive treatise of arrow poisons, and some 20 articles in psychopharmacology (Holmstedt and Liljestrand, 1963). In 1924 he summarized the field of psychoactive drugs in his book "Phantastica" (reprinted in 1964).

In 1887 Lewin visited the U.S. and Canada. His trip resulted in a handwritten manuscript of more than 300 pages. This family property was never printed and was not intended to be. It was written as a gift to his wife. Lewin's itinerary took him to the great lakes, to San Francisco, Detroit, Washington and back. He was especially interested in visiting San Francisco's China Town to see the smoking of opium, but the city he really longed to visit was Detroit. He arrived there on September 16th, 1887:

> My first errand was, of course, a visit to Parke Davis. We drove along a splendid wide avenue bordered by residences with beautiful gardens. Soon we were marvelling at a grand extensive building adorned with sand-stone. This building, which belongs to the company, is not yet fully finished. We enter the office where there work well over fifty book-keepers, male and female, cashiers, clerks, stenographers, etc. Mr. Wetzell showed us round the factory and the printing-shop — I had not expected such a magnitude and such a skilled exactitude of workmanship .... In short, the manufacture of pharmaceutical preparations is worthy of the American genius for machinery and for exactitude and cleanliness of use. Whatever I received — preparations, drugs, etc. — you will see for yourself when everything arrives in Berlin.

Among other things he received more material of the "muscale buttons", which he had promised to investigate. The only item referring to Lewin's visit in the Parke-Davis' papers is a brief note in Mr. Wetzel's handwriting: "Muscale Button given to L. Lewin, Berlin, for investigation. H. W. Sept 17/87."

After his return to Germany, Lewin was not long in investigating the properties of the drug. Using various extraction methods, he obtained a basic, syrupy substance which he called anhalonine. He used this "substance", which was in fact a crude mixture of alkaloids, in animal experiments and found to his surprise that it was intensely poisonous (Lewin, 1888a).

Realizing the importance of plant identification, Lewin turned over some of his drug material to the botanist Hennings, at the Royal Botanical Museum in Berlin. An enthusiastic letter from Hennings to Lewin, dated December 3rd, 1887, and now published for the first time, reads as follows:

Berlin, Roy. botan. Mus. Dec. 3 1887.

Hochgeehrter Herr Doctor!

> I am afraid that you might let pass the proposed 8 days before renewing your esteemed visit to our museum. I cannot wait to let you know that I have yesterday examined your cactus carefully and that I came upon very gratifying results. I was lucky indeed, as I found, hidden in the haircushions, a beautifully preserved blossom. The plant belongs to the Melocacteae, as I told you right in the beginning, to the genus *Anhalonium*, of which only 6 species are known from Mexico.

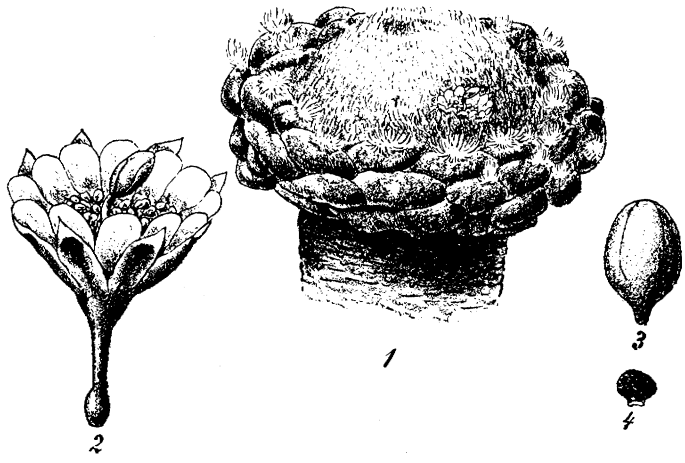

Abbildung 92. Anhalonium Lewinii.

Fig. 1. Anhalonium Lewinii. Pflanze mit abgeschnittener Wurzel, nach einem aufgekochten, vorher trockenen Exemplar (in natürlicher Grösse). Fig. 2. Blüte, 3 mal vergrössert. Fig. 3. Frucht, ebenso. Fig. 4. Same, ebenso.

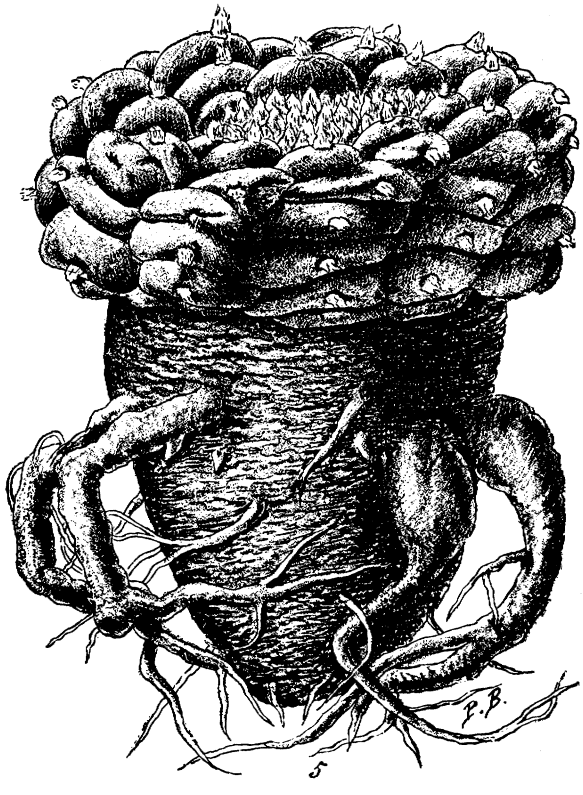

Abbildung 93 (Fig. 5). Anhalonium Williamsii Lem., in natürlicher Grösse, nach einem lebenden Exemplar des Berliner Gartens.

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Fig. 5. Illustration from Hennings' paper "*Eine Giftige Kaktee, Anhalonium Lewinii n. sp.*" (1888). The upper figure was drawn from a boiled specimen of the "muscale buttons" which Lewin had given Hennings.

> The species that we have before us does not correspond in the shape of its body, in the color of its tuft of hair, in the form of its blossom to any of the described 6 species, so that, without any doubt, we have to do with a new species which I will take the liberty to name for you, as you are actually the discoverer of the plant, as well as of its toxic nature. — I enclose an accurate description of a boiled specimen of the plant. It is only the structure of the stigma and the pistil which I have not yet examined, as I did not want to destroy the only blossom. However, it is possible that I find corresponding parts on other specimens. — The genus is characterized by a milky substance, which I have also observed in *Mamilaria* etc. The milky juice resembles that of the cactus-like Euphorbiaceae, at least outwardly. It is white, thick, curdles very quickly. Its taste I do not know yet, but shall investigate tomorrow morning. — Perhaps you will be privileged to observe similar poisonous matter in other specimens. Luckily you will find in our garden one of the largest collections of cacti in the world. — I will like to discuss with you publication of the description. — Hoping that you will honor us in the near future with your visit,
>
> With kind regards
> Hochachtungsvoll
>
> P. Hennings

On February 10, 1888, Hennings presented his paper "Eine giftige Kaktee, *Anhalonium Lewinii* n. sp." to the Botanical Society of Berlin. He considered the new species to be close to *Anhalonium williamsii*, and based his description on the dried "muscale buttons" supplied by Lewin (Hennings, 1888). This was the first identification of the drug on the species level (Fig. 5).

Shortly afterwards, Lewin published the first account of his chemical and pharmacologic studies of the new drug. He said in his summary:

> It has been proven for the first time that a cactus can possess an extraordinarily high toxicity. It will now be appropriate to elucidate the chemistry of this *Anhalonium* and then go further with the investigation of other species of *Anhalonium*. One must, however, also investigate to what purpose and to what extent these "Muscale buttons" are used as stimulants (Lewin, 1888a; 1888b).

This was the first published report of alkaloids in the Cactaceae, and Lewin, anticipating the wide-spread interest this would awaken, tried to monopolize further investigations by saying:

> Der volle Abschluss der Untersuchung wird sich erst in einiger Zeit ermöglichen lassen und behalte ich mir ausdrücklich bis dahin die weitere Bearbeitung dieses Gegenstandes vor.

In the meantime, Parke-Davis had found a more reliable source of the "buttons". On May 29, 1888, Mrs. Anna B. Nickels of Laredo, Texas, wrote to Parke-Davis reporting that she had "3000 plants growing in my garden, and can collect all I can find sale for" (Bender, 1968). Mrs. Nickels had a large private collection of cacti and also a nursery of her own in Laredo. She collected cacti on a large scale for the American and European trade (Mitich, 1971). Mrs. Nickels was long considered to be the first supplier of "mescal buttons" for scientific study, but Slotkin (1955, p. 222, note 7) rejected this and pointed out that Briggs was the pioneer (cf. Bender, 1968).

Thus, only a year after Briggs' initial paper, the "muscale buttons" had been botanically clarified and an adequate source of them found. Furthermore, chemical and pharmacological investigations were underway. On this

foundation, Parke-Davis now introduced the cactus in medical practice. The company's catalogue of February 25, 1889, included the tincture of *Anhalonium Lewinii*, said to possess "marked physiological action similar to strychnine". For the next few years the drug was experimented with as a cardiac stimulant and tonic, and in treating angina pectoris (Bender, 1968; Prentiss and Morgan, 1896).

The Anhalonium Lewinii Controversy

Following Hennings' description of *Anhalonium lewinii*, several botanists began studies of the genus *Anhalonium*. *A. lewinii* and *A. williamsii* were variously referred to *Echinocactus*, *Mammillaria* and *Ariocarpus* (Michaelis, 1896; Anderson, 1969). In 1894 Coulter revised the genus *Anhalonium* and erected the new genus *Lophophora*, including *L. williamsii* and *L. williamsii* var. *lewinii*. Some of the specimens examined had been collected by Mrs. Nickels in Texas. Coulter added: "Mrs. A. B. Nickels reports that the Indians use the plants in manufacturing an intoxicating drink, also for "breaking fevers", and that the tops cut off and dried are called "mescal buttons". Regarding the distribution of *Lophophora*, Coulter said: "*L. williamsii* is reported from southern Mexico, but so little is known of the distribution of these plants that their eastern Mexican range is conjectural."

In a commentary on Coulter's paper, Rusby (1894) doubted the correctness of reducing *A. lewinii* to varietal rank and said: " . . . we shall prefer to define Muscale Buttons as the body of *Lophophora Lewinii* . . . .".

Anthropological and ethnographical details were likewise accumulating. James Mooney, of the U.S. Bureau of Ethnology, in a newspaper report of 1892 described the ceremony of "eating the mescal" of the Kiowa Indians[11] (Mooney, 1892a), and described a Kiowa "mescal rattle" used in the "mescal ceremony" (Mooney, 1892b).

In Mexico, the Norwegian explorer Carl Lumholtz had observed the use of peyote among the Tarahumara Indians (Lumholtz, 1894) and sent "mescal buttons" to the Gray Herbarium of Harvard University (Schultes, 1937b).

Interest in "mescal buttons" spread also among chemists. In 1889, Rudolf Boehm, Professor of Pharmacology in Leipzig, received a small amount of *Anhalonium lewinii* from a German doctor, F. Tischer, living in Mexico. According to Dr. Tischer, the native name was "pellote". Two years later, 42 kg of "pellote" was received in Leipzig, and this material was given to Arthur Heffter, Boehm's assistant (Heffter, 1894a).

Arthur Heffter (1860-1925) was born in Leipzig. He first studied chemistry and received his Ph.D. in Greifswald in 1883. After some years in agricultural chemistry he switched to study medicine in Leipzig, at the same time working in the laboratory of Boehm. In 1890 he received his M.D. in Leipzig. In the following years he held positions in various universities until in 1908 he became professor of pharmacology at the University of Berlin, where he stayed until his death. Among other things he studied anthelmintics, arsenic, and strophanthine (Holmstedt and Liljestrand, 1963).

The Mexican "pellote" material given to Heffter was soon shown to belong not to *A. lewinii* but to *A. fissuratum* (now known as *Ariocarpus fissuratus*). However, at the "Gartenbauausstellung" in Leipzig in 1891, he was able to purchase both *A. lewinii* and *A. williamsii* from various cactus dealers. He was also informed by the cactus collector Matthsson that the true "pellote" was *A. williamsii* and that Matthsson considered *A. lewinii* to be only a variety of this species (Heffter, 1894a).

[11] According to Safford (1915), Mooney reported the ceremonial use of "mescal" in a paper read before the Anthropological Society of Washington on November 3, 1891.

Fig. 6. Arthur Heffter (1860-1925).

Heffter now systematically studied the *Anhalonium* species at his disposal. From *A. williamsii* he isolated large amounts of a new alkaloid which he called pellotine. He found in self-experiments that pellotine produced sedation and sleepiness. No other alkaloids were found in this plant.

A. lewinii yielded two alkaloids and the presence of a third compound was also indicated. These alkaloids were all different from pellotine in animal experiments (Heffter, 1894a, 1894b).

Since 1888 Lewin had published nothing on *A. lewinii.* It would seem, however, that rumours of Heffters's research activities had reached him. Late in 1893 he asked the Merck laboratory in Darmstadt to help him with the cactus work because his private laboratory had no facilities for large-scale drug extraction. This is evident from a letter to Lewin, dated November 30, 1893, and signed by E. Merck: "Ich bin gerne bereit Ihr Anhalonium-Material auf Alkaloid zu verarbeiten und ersuche Sie mir dasselbe bei Gelegenheit senden zu wollen."

The *Anhalonium* material was received early in 1894 by Merck and given to the chemist Kauder, who crystallized anhalonine (Merck, 1895; Kauder, 1899). Lewin now studied the pure anhalonine and rushed to report the properties of this alkaloid. He also confirmed the presence of pellotine in *A. williamsii,* which had been found by Heffter, and included in the paper were preliminary studies of five *Mammillaria* species. Lewin also complained about the difficulties in obtaining sufficient amounts of these expensive plants without government grants (Lewin, 1894a).

The same year he published a more botanically oriented article, citing several of the older Mexican authors on the use of peyote. He strongly argued that chemical differences, such as those found by him and Heffter

between *A. lewinii* and *A. williamsii*, should be taken into account in plant taxonomy (Lewin, 1894b).

By the end of 1894, *A. lewinii* had thus been found to contain three alkaloids, one of them being anhalonine. *A. williamsii* had yielded only pellotine. (A discussion of this analysis is found on p. 46.)

Lewin was obviously not happy that Heffter had entered the scene. However, things were to become worse. On March 7, 1895, Karl Schumann, the renowned cactus botanist, read a paper on poisonous cacti before the pharmaceutical society of Berlin. He asserted that *A. lewinii* and *A. williamsii* could not be considered as two separate species. He discussed and discarded the morphological differences found by Hennings, and he also maintained that a botanist could not rely on the chemical differences, as suggested by Lewin (Schumann, 1895).

An abstract of Schumann's lecture appeared in the *Pharmaceutische Zeitung*, and Heffter's results were very briefly and incorrectly mentioned compared to Lewin's. This annoyed Heffter, who immediately sent a letter to the editor (published on April 6), reviewing Lewin's and his own contributions in this field. Heffter recognized Lewin's priority but also showed that he, Heffter, had been first to isolate a *pure* alkaloid from "pellote" (Heffter, 1895).

On May 22, an angry reply by Lewin appeared in the pages of the *Pharmaceutische Zeitung*. He briefly declared: "Ich habe weder Zeit noch Lust, Herrn Heffter zur Erkenntniss meiner Untersuchungsergebnisse zu verhelfen". ("I have neither time, nor do I feel inclined, to make Mr. Heffter understand the results of my research.") (Lewin, 1895). With this, Lewin seems to have left his studies of *Anhalonium lewinii*. The difficulty in obtaining material (Parke-Davis had apparently lost interest in his research), the botanical controversy and Heffter's successful isolation of several alkaloids must have been the deciding factors.

He supplied various other research workers with drug material, however — e.g., Guttmann (1914) received anhalonine and Jaensch (1920) "mescal buttons". Merck consulted him to verify that a shipment of "muscale buttons" did correspond to *A. lewinii* (letter from E. Merck to L. Lewin, April 14, 1896).

Later in life he briefly returned to the "mescal buttons" in his books about "Phantastika" (new edition, 1964) and the monumental work on poisons and poisonings (1929). Even in these later publications he maintained his concept of *A. lewinii*. He had also developed a dislike for Heffter, and this was of lasting character. When Heffter eventually came to Berlin, the long-standing grudge between the two men was obvious even to their pupils:

> Lewin did not like Heffter and Heffter did not like him. They had very different opinions on many things — this concerned particularly *Anhalonium Lewinii* (Peyotl) on which Heffter also had done work. It was a priority competition between the two. I don't remember it exactly, but I have the feeling that it was something of the sort. Lewin was more the artist and interested in the social implications of these substances. Heffter was not very verbal, awkward, frankly in the presentation of his material. On the other hand, here was this tremendously stimulating, flamboyant orator Lewin, who carried away his audience with his enthusiasm. The atmosphere fused into the most extraordinary experience every time we went to that place to listen to his lecture, and you did that in spite of the fact that you didn't have to — it was enough had you followed only Heffter's lectures. I went to Heffter's lectures, of course, and I was bored. Lewin lectured the first time and I was captured — I went there every time (Krayer, 1963).

Lack of material had been experienced in the United States too. In 1894, however, Prentiss and Morgan (1895) of the Medical Department of Columbian University in Washington obtained a large supply of mescal buttons through James Mooney, "agent among the Indians". They described six experiments in man with the crude drug. "The production of visions" was the most interesting effect found, and the authors concluded that the action of *Anhalonium lewinii* was not identical with that of any other drug. Except for Briggs' early (and somewhat dubious) self-experiment, these were the first reported studies of the drug in man.

The following year Mooney (1896), from the U.S. Bureau of Ethnology, described "The Mescal Plant and Ceremony" among the Kiowa Indians. Mescal buttons collected by Mooney were also studied in the U. S. Department of Agriculture by Ewell, who reported the isolation of three alkaloids (Ewell, 1896) and said: "It is to be hoped that American scientists will not leave the task of exploring this promising field entirely to workers beyond the sea, considering our proximity to much of the necessary material."

However, beyond the sea, Heffter had already left the American scientists far behind. He now fully described the isolation of anhalonidine, mescaline, anhalonine and lophophorine. This time the material of *Anhalonium lewinii* had been supplied by Parke, Davis & Co. in Detroit (Heffter, 1896a, 1896c).

He further showed the hypnotic effects of pellotine (Heffter, 1896b), and several authors reported on clinical tests with this alkaloid. First of them was Friedrich Jolly (1896a, 1896b), the brother-in-law of Heffter's teacher, Rudolf Boehm. Jolly, Pilcz (1896), Hutchings (1897) and others found pellotine to be of interest as a sedative and hypnotic. There were side-effects, such as vertigo, but the authors recommended further testing. For some time pellotine was produced by Boehringer & Sohn in Mannheim, but sufficient supplies of *A. williamsii* could not be found. A preparation from *A. lewinii*, *Extr. Anhalonii Lewinii fluidum* was brought on the German market in 1896 by Merck (Merck, 1897).

In England a medical doctor, Mitchell (1896), and an author, Ellis (1897, 1898), explored the inner depths of "mescal intoxication". Their descriptions of the wonderful visions served to spread the interest in peyote far beyond scientific circles. Ellis (1897) prophesied: ". . . there is every likelihood that mescal will become popular. It certainly has a great future before it with those who cultivate the vision-breeding drugs."

Among those cultivating *Anhalonium lewinii* were the Huichol Indians of Mexico, as reported by Lumholtz (1898).[12] Lumholtz sent some "buttons" to Heffter, who now gave a full account of his pharmacological studies (Heffter, 1898a,b). By testing the crude drug, the total alkaloids, and the individual alkaloids in gruesome self-experiments, he had found the active component. Since extracts of Heffter's classic paper (1898a) have been published earlier (Holmstedt and Liljestrand, 1963; Holmstedt, 1967), only brief mention will be made here. The whole drug produced colour visions, nausea, headache, and bradycardia. The total alkaloids gave the same effect, but which one produced the visions? On November 23rd, 1897, Heffter performed the conclusive experiment. "The results . . . show that mescaline is exclusively responsible for the major symptoms of mescal poisoning."

The next year anhalamine, a new alkaloid, was isolated from *A. lewinii* in the Merck laboratory by Kauder (1899). Kauder also reported the finding of

[12]"This plant is also used to a certain extent by the Cora Indians, who buy it from the Huichols. Both tribes cultivate the plant on a very small scale; liliputian gardens, or tiny patches of land, being enclosed with a stone wall for the purpose." (Lumholtz, 1898).

pellotine in "mescal buttons" and at first suggested that this could be due to an admixture of *A. williamsii* in the drug material. *A. williamsii* investigated by Heffter (1894a) and Lewin (1894a) was known to contain pellotine as the major and almost only alkaloid. But when Kauder studied *A. williamsii* he found the same alkaloids as in "mescal buttons", which until then had been thought to derive from *A. lewinii* only (Kauder, 1899; Merck, 1900). Kauder concluded that *A. williamsii* could *not* be the cactus that contained almost only pellotine and added: "Die Verhältnisse scheinen mir weiterer Klärung zu bedürfen, welche erst dann möglich ist, wenn es glückt, diejenige Kaktee zu beschaffen, welche nur Pellotin enthält. Trotz vieler Mühe is das bis jetzt nicht gelungen." ("The circumstances seem to me to call for further clarification, which will only be possible when we succeed in obtaining that cactus, which contains only pellotine. In spite of great effort, this has not yet been accomplished.") (Merck, 1900). The chemotaxonomical problem of the pellotine-containing *Anhalonium* seems not to have been further investigated. Instead, the finding that mescaline is the active hallucinatory agent of peyote directed attention to the chemistry and pharmacology of this compound.

The physiological effects of the alkaloids were further studied by Dixon (1899-1900) in London, and Heffter, who had by now moved from Leipzig to Bern, continued with chemical studies. In 1901 he suggested that mescaline was in fact 3,4,5-trimethoxybenzylmethylamine (Heffter, 1901), and he also encouraged a pupil to study the effect of the then known cactus alkaloids on the frog's heart (Mogilewa, 1903). Heffter's last paper on cactus alkaloids appeared in 1905, when synthetic 3,4,5-trimethoxybenzylmethylamine was shown *not* to be identical with mescaline (Heffter and Capellmann, 1905).

With this paper the first wave of chemical interest in peyote expired. Some papers on the Indian use of peyote followed, as well as reports of experimental hallucinations from taking the drug (e.g., Guttmann, 1914). In 1915, Safford published his classic paper "An Aztec Narcotic", in which he erroneously identified peyote with the sacred, intoxicating mushroom of the Aztecs. This identification was unfortunately accepted and has until recently been firmly established in the literature (Safford, 1915).

The revival of interest in peyote was to come after the First World War, when on December 12, 1918, the Austrian chemist Ernst Späth reported that the correct structure for mescaline was 3,4,5-trimethoxyphenylethylamine (Späth, 1919). Heffter had thus been remarkably close to the correct structure.

A word remains to be said about the botany of *Anhalonium lewinii* and *A. williamsii.* In 1898 Schumann reached the conclusion that there was only *one* species, which should be called *Echinocactus williamsii.* However, he recognized two "chemical forms": *pellotinica* and *anhaloninica.* Of special interest is his citation of a letter from Heffter: "Ich habe im Laufe der letzten 4 Jahre grosse Posten von frischen *Anhalonium* verarbeitet von je 200, 300, ja 1000 Stück, die teils direct aus Mexico, teils durch Vermittlung deutscher Händler bezogen waren. Dabei zeigte sich, dass jede Sendung immer *einheitlich* war, sie lieferte entweder nur *Pellotin*, bestand also ausschliesslich aus *A. Williamsii*, oder sie lieferte Mezkalin, *Anhalonin* etc., *aber kein Pellotin*, bestand also nur aus *A. Lewinii.*" ("During the last 4 years I have worked up large amounts of fresh *Anhalonium*, of 200, 300, even 1000 plants, that were purchased in part directly from Mexico, in part through the help of German dealers. It was observed, that every shipment was always *uniform*, either yielding only *Pellotine* and thus consisting of *A.*

Fig. 7. The distribution of *Lophophora*. *Lophophora williamsii*, the northern species, is found from southern Texas southwards into Mexico, ranging into San Luís Potosí. *Lophophora diffusa*, "the southern type", is only found in a limited area in Querétaro. Redrawn from Anderson (1969) with the author's permission.

Williamsii exclusively, or yielding Mescaline, *Anhalonine* etc., but not *Pellotine*, thus consisting only of *A. Lewinii.*") Schumann concluded, that the two chemical forms *must also be local forms* (Schumann, 1898), and he maintained this view in his "Gesamtbeschreibung der Kakteen" (1903):

> Sehr bemerkenswert ist übrigens, dass sich beide Formen geographisch ausschliessen; an derselben Örtlichkeit scheint immer nur eine derselben zu gedeihen. Selbst die umfangreichsten Importe haben niemals eine Mischung gezeigt. (It is also very remarkable, that both types exclude each other geographically; only one of them seems to grow in the same place. Even the most extensive imports have never turned out to be mixtures.)

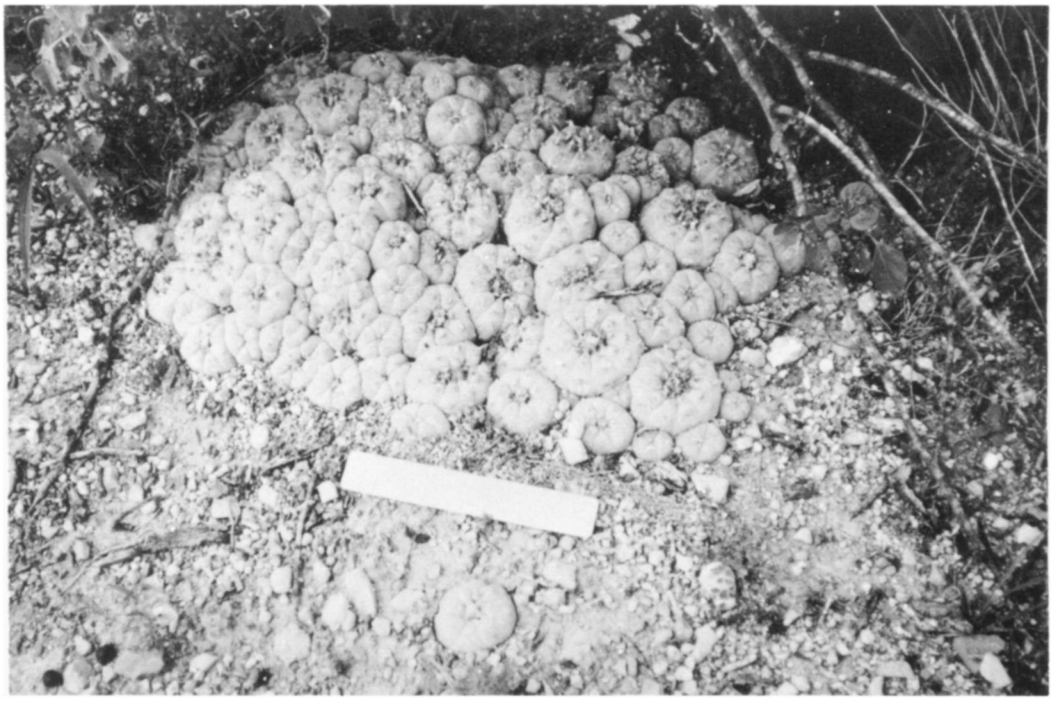

Fig. 8. *Lophophora williamsii* (Lem.) Coulter. El Huizache, San Luís Potosí. Length of ruler 15 cm. Photograph by Jan G. Bruhn.

Fig. 9. *Lophophora diffusa* (Croizat) Bravo. North of Vizarrón, Querétaro. Photograph by Jan. G. Bruhn.

Alas, Schumann's conclusions were soon forgotten. The name *Lophophora* was favored for the genus, and the number of species and varieties since suggested (cf. Anderson, 1969) is sufficient to make anyone feel perplexed. When Lewin summarized the knowledge of peyote in 1924, he rightfully remarked: ". . . the chemical and biological investigations proved very valuable, whereas the flood of botanic research was with a few exceptions unproductive" (Lewin, 1964).

TAXONOMY

The confused state of *Lophophora* taxonomy was not brought in order until Bravo (1967) and Anderson (1969) published extensive studies of the genus, based on field data. Anderson (1969) has also published a distribution map of *Lophophora*, which we have reprinted here (Fig. 7). As outlined by Bravo (1967) and Anderson (1969), the genus consists of two species, *Lophophora williamsii* and *L. diffusa*. *L. williamsii* (Fig. 8) has a widespread and highly variable population occurring from Texas southwards to San Luís Potosí. *L. diffusa* (Fig. 9), on the other hand, has a small population restricted to the state of Querétaro. Both Bravo (1967) and Anderson (1969) include *Anhalonium lewinii* Hennings as a synonym of *Lophophora williamsii* and also discuss this conclusion thoroughly. In the opinion of Anderson (1969), "it is not possible to find single populations that correspond to the characters attributed to Henning's *Anhalonium lewinii* and that are clearly distinct from *L. williamsii*". This seems to be the last word in this old botanical controversy. The following description of the genus and key to the species have been cited from Anderson (1969).

Lophophora Coulter, Contr. U.S. Nat. Herb. 3: 131. 1894.

TYPE species: *L. williamsii* (Lemaire) Coulter.

Plants low, with long fusiform roots. Stems solitary or in clusters arising from the same root system, usually rounded above, depressed in the centers; blue-green, yellow-green, and occasionally appearing reddish green; 2-7 cm high, 4-12 cm in diam. Areoles usually linearly arranged along ribs or at the apices of hump-like tubercles or podaria, each bearing a tuft of soft, yellowish or whitish trichomes from which the flowers arise, 8-15 mm apart, 1-5 mm in diam; spines absent except in seedlings and then only rudimentary. Flower 1-2.2 cm in diam, 1-2.4 cm long; outer perianth segments with greenish midribs and greenish pink or whitish margins, the largest ones elliptical, 3-12 mm long, 1-3 mm broad, mucronate, marginally minutely ciliate distally; inner perianth segments pink, white, or rarely yellowish white, sometimes with greenish midribs, the largest ones elliptical, 8-22 mm long, 2-4 mm broad, mucronate or occasionally attenuate, margins ciliate or entire; filaments white; anthers yellow; pollen ± spheroidal, 0-18 colpate, 14.9-63 μ diam; style white, 5-14 mm long; stigmas 4-8 (rarely 3), 1-3 mm long, white though occasionally pinkish; ovary naked. Fruit pinkish red and fleshy at first, becoming brownish white and dry at maturity, naked, clavate, 15-20 mm long, 2-3.5 mm in diam, with the umbilicus large or the perianth parts persistent, emerging rapidly from within the trichomes at maturity. Seeds black, tuberculate (verrucose), pyriform, 1-1.5 mm long, 1 mm broad; hilum large and flattened; cotyledons coalescent.

Key to the Species

Plants blue-green, usually with well-defined ribs and furrows; tufts of trichomes usually equally spaced on the ribs; flowers pinkish or rarely whitish; not in Querétaro. 1. *L. williamsii.*

Plants yellow-green, usually lacking well-defined ribs and furrows; tufts of trichomes usually unequally spaced on prominent podaria; flowers commonly whitish to yellowish white; Querétaro. 2. *L. diffusa.*

1. L. WILLIAMSII (Lemaire) Coulter, Contr. U.S. Nat. Herb. 3: 131. 1894.

Echinocactus williamsii Lemaire ex Salm-Dyck in Otto & Dietr., Allgem. Gartenzeit. **13**: 385. 1845.
Anhalonium williamsii Rümpler in Förster, Handb. Cact. ed. 2. 233. 1886.
Anhalonium lewinii Hennings, Gartenflora **37**: 410. 1888.
Mammillaria williamsii Coulter, Contr. U.S. Nat. Herb. **2**: 129. 1891.
Lophophora williamsii Coulter, Contr. U.S. Nat. Herb. **3**: 131. 1894.
Ariocarpus williamsii Voss, Vilmorin Illustrirte Blumengärtneri 368. 1894.
Echinocactus lewinii K. Schumann, Nat. Pflanzenfam. **3** Abt. 6a: 173. 1894.
Lophophora williamsii var. *lewinii* Coulter, Contr. U.S. Nat. Herb **3**: 131. 1894.
Lophophora lewinii Rusby, Bull. Pharmacy **8**: 306. 1894.
Mammillaria lewinii Karsten, Flora Deutsch. ed. 2. **2**: 457. 1895.
Echinocactus williamsii var. *lutea* Rouhier, Trav. Labouret Mat. Med. Pharm. Galén **17**(5): 65. 1926.
Lophophora echinata var. *lutea* Croizat, Desert Plant Life **16**: 44. 1944.
Lophophora echinata Croizat, Desert Plant Life **16**: 43. 1944.
Lophophora williamsii var. *lutea* Soulaire, Cactus et Médicine 121. 1947.
Lophophora lutea Backeberg, Die Cactaceae **5**: 2901. 1961.
Lophophora williamsii var. *echinata* H. Bravo, Cact. Sucul. Mex. **12**(1): 12. 1967.

2. L. DIFFUSA (Croizat) Bravo H., Cact. Sucul. Mex. **12**: 13. 1967.

Lophophora echinata var. *diffusa* Croizat, Desert Plant Life **16**: 44. 1944.

In addition to the above, several names of uncertain status have been discussed by Anderson (1969).

EXPERIMENTAL

Plant Materials

"*Muscale Buttons*" (2.83 g) were obtained from the Gray Herbarium, Harvard University, and were labelled: "*Anhalonium Lewinii*" Hennings, "muscale buttons", Rusby 1887 — S. Mexico. The drug material was identified as *Lophophora williamsii* (Lemaire) Coulter at the herbarium of Pomona College, Claremont, California, by Dr. E. F. Anderson, April 25, 1961. (cf. figs. 2 &3).

Lophophora williamsii (Lemaire) Coulter was purchased from K. Uhlig, Rommelshausen, F. R. G., and from W. Uebelmann, Wohlen, Switzerland. *Lophophora diffusa* (Croizat) Bravo was collected north of Vizarrón, Querétaro, on June 29, 1971, by one of the authors (J.G.B.) and Sr. Hernando Sánchez-Mejorada, Departamento de Botánica, Instituto de Biología. Universidad Nacional Autónoma de México, Mexico City, who also identified the plants. Fifty plants of *L. diffusa* were collected, weighing in all 4.900 g. Reference cacti are maintained in the greenhouse of the Department of Pharmacognosy, Faculty of Pharmacy, Uppsala.

Prior to the isolation of alkaloids from *Lophophora williamsii*, the tops of the plants were separated to make possible a comparison of the alkaloid content of top and root. The tops were further cut in slices, half of which

were immediately extracted. The remaining slices were dried under a heating lamp (not over 40°C) for 2 days and then allowed to air-dry in the laboratory for 2 weeks, thus forming "new mescal buttons". The water content was found to be 89%. Before extraction of the alkaloids, the dried materials were ground with sand in a mortar to a fine powder.

Isolation of Alkaloids

The fresh plant material was cut in pieces and homogenized in ethanol. After standing overnight at +5°C and after filtration, the ethanol extract was evaporated to dryness under reduced pressure at room temperature. The residue was dissolved in 3% acetic acid and washed with chloroform. The chloroform extract was discarded and the water phase was alkalinized with concentrated ammonia (pH 9) and extracted twice with chloroform and once with chloroform-ethanol (3:1). The combined chloroform extracts were evaported to dryness, dissolved in a small volume of chloroform and passed through an acid celite column as earlier described (Lundström, 1970). The purified alkaloid extract was evaporated to dryness, weighed, and then separated into phenolic and non-phenolic alkaloids by passing through an anion exchange column (Agurell, 1969).

The dried plant materials were powdered and mixed with water to a slurry. This was alkalinized with concentrated ammonia to pH 9-10 and extracted for several hours with chloroform (twice) and once with chloroform-ethanol (3:1). The combined chloroform extracts were evaporated and the residue dissolved in chloroform. All subsequent steps were the same as for fresh plant material. The results are presented in Table I.

Isolation of Pellotine from Lophophora diffusa

Thin-layer (tlc) and gas chromatography (gc) of the phenolic alkaloid fraction of *Lophophora diffusa* showed the existence of one major alkaloid, which could be crystallized as the hydrochloride, m.p. 236-241°C, and the picrate, m.p. 169-171°C. Reported m.p. of pellotine picrate 167-169°C (Späth, 1922). Identical IR spectrum and chromatographic behavior (tlc, gc) proved the identity of the isolated compound with authentic pellotine hydrochloride.

Thin-layer and Gas Chromatography

Except for the use of precoated tlc-sheets (Woelm, Silica Gel F), the conditions for tlc and gc were essentially the same as in earlier studies (Lundström and Agurell, 1967, 1968; Agurell et al., 1971; Bruhn and Bruhn, 1973). Identification of alkaloids was based on comparison with reference materials, using tlc, gc and gc-ms.

Gas Chromatography — Mass Spectrometry

This technique (gc-ms) has been described earlier (Holmstedt and Lindgren, 1967; Agurell, 1969). The instrument used was an LKB 9000 gas chromatograph — mass spectrometer. The ion source was 270°C, the electron energy 70 eV and the electron ionization current 60 μA, respectively.

RESULTS AND DISCUSSION

I. The Old Rusby Material

The persistence of alkaloids in plant material has been observed by several investigators. Raffauf and Morris (1960) reported a positive test for alkaloids

TABLE I

DISTRIBUTION OF ALKALOIDS

Plant Material*	Alkaloids % (total)	Alkaloids % phenolic	Alkaloids % non-phenolic
Lophophora williamsii (Lemaire) Coulter	0.47†	60‡	40‡
Roots	0.20	67	33
Tops	0.93	58	42
"New Mescal Buttons" (Dried Tops)	8.41§	64	36
"Old Mescal Buttons" (1887)	8.86	65	35
Lophophora diffusa (Croizat) Bravo	0.90‖	98	2

* All plant material was fresh, except the two "mescal button" samples.

† Whole plants. Lundström (1971a) reports an average of 0.4%.

‡ The percentages of separate compounds of the alkaloid fraction given by Lundström (1971a), give a total of 57.5% phenolic and 42.5% non-phenolic alkaloids.

§ Upon drying, the fresh tops lost 89% water (see Experimental).

‖ Whole plants.

on a sample of plant material estimated to be 1300 years old. Neither plant material nor alkaloids were, however, identified.

In a screening program for the alkaloids of Asian *Strychnos* species, more than 200 samples from herbarium collections were studied by tlc and gc (Bisset and Phillipson, 1971). The results obtained with *S. nux-vomica* L. and *S. wallichiana* Steud. ex DC. (*S. colubrina* L.) are particularly interesting in that the alkaloid composition of the leaf and seed, irrespective of age (up to 300 years old) appeared to be unchanged.

The unequivocal identification of alkaloids in old plant material has been hampered by the small amounts of original material available from herbarium sheets, drug collections, etc. The arrival of modern analytical microtechniques has, however, solved this problem and recent research has given some interesting results. For example, a 115-year-old sample of the narcotic liana *Banisteriopsis Caapi* collected by Spruce in the Amazon was found by gc-ms to contain the alkaloid harmine (Schultes, Holmstedt and Lindgren, 1969).

Among other items found in a medicineman's tomb in highland Bolivia, bundles of *Ilex Guayusa* leaves could be identified (Schultes, 1972a). These leaves were ^{14}C-dated to around A. D. 375, and analysis showed that they still contained caffeine (Holmstedt and Lindgren, 1972).

In view of these findings, it is not surprising that alkaloids are still present in the "muscale buttons" that Rusby sent to Watson in 1887. As seen in Table 1, both the percentage of total alkaloids and the proportions between phenolic and non-phenolic alkaloids are almost the same as for recently dried tops of *Lophophora williamsii*, "new mescal buttons".[13]

There are, however, some quantitative and qualitative differences between the old and the new material. Mescaline is still present in the Rusby material and was unequivocally identified by gc-ms, but when equal amounts of the non-phenolic alkaloid fractions were compared (Fig. 10), the mescaline

[13] Comparison of the "new mescal buttons" (Fig. 10, lower panel) with fresh *L. williamsii* (Fig. 14, lower panel) shows no significant differences.

Fig. 10. Gas chromatographic comparison of alkaloid fractions from "mescal buttons". 5% SE-20 on Gas Chrom P. Low magnification. Upper panel: Non-phenolic alkaloid fraction from the "old mescal buttons" (1887). Lower panel: Non-phenolic alkaloid fraction from "new mescal buttons", prepared from fresh plants of *Lophophora williamsii*.

Peak 1 = mescaline, peak 2=anhalonine, peak 3=lophophorine.

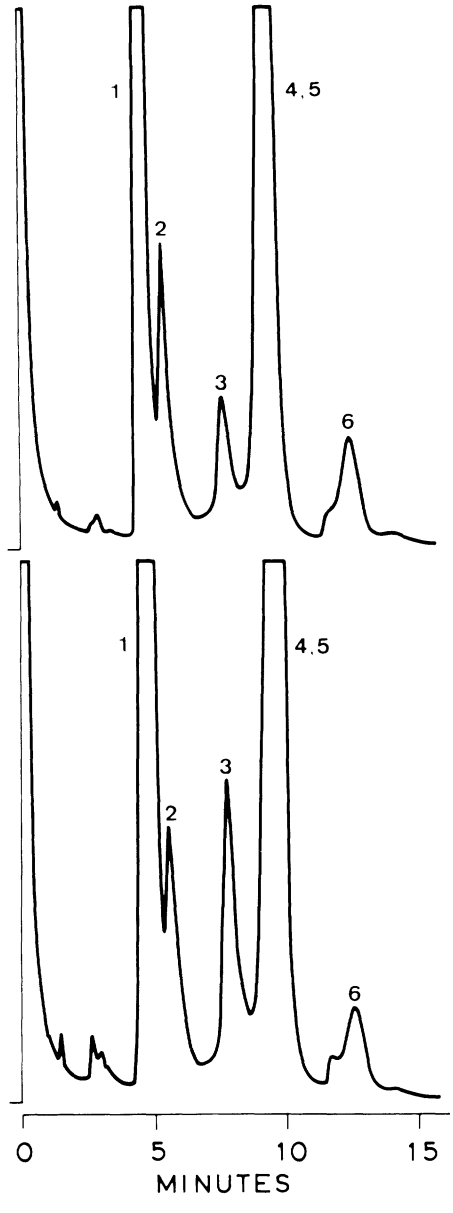

Fig. 11. Gas chromatographic comparison of alkaloid fractions from "mescal buttons". 5% SE-30 on Gas Chrom P. Low magnification. Upper panel: Non-phenolic alkaloid fraction from the "old mescal buttons" (1887). Lower panel: Non-phenolic alkaloid fraction from "new mescal buttons", prepared from fresh plants of *Lophophora williamsii*.

Peak 1 = mescaline, peak 2 = *N*-methylmescaline, peak 3 = anhalinine, peak 4 = anhalonine, peak 5 = lophophorine, peak 6 = peyophorine.

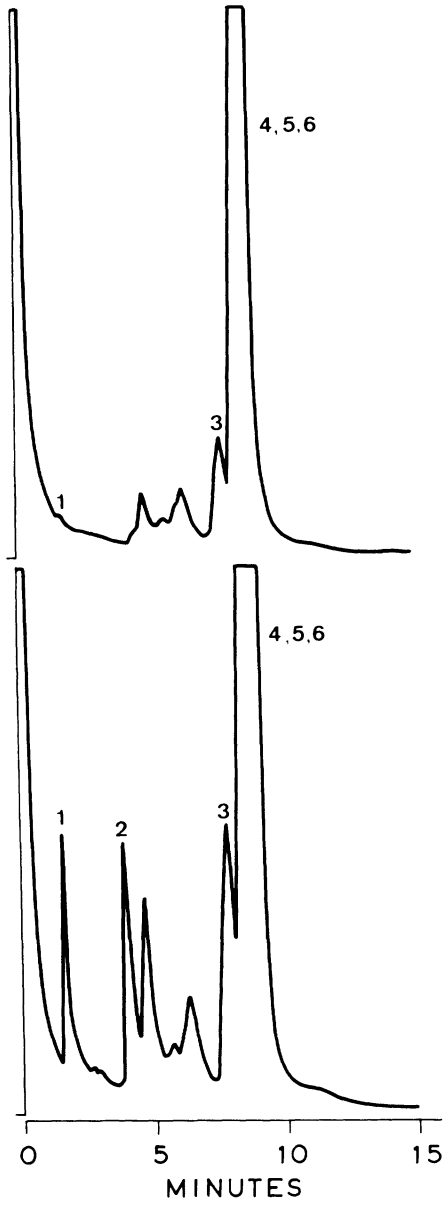

Fig. 12. Gas chromatographic comparison of alkaloid fractions from "mescal buttons". 5% SE-30 on Gas Chrom P. Upper panel: Phenolic alkaloid fraction from the "old mescal buttons" (1887). Lower panel: Phenolic alkaloid fraction from "new mescal buttons", prepared from fresh plants of *Lophophora williamsii.*

Peak 1 = hordenine, peak 2 = 3-hydroxy-4,5-dimethoxy-phenethylamine, peak 3 = anhalidine, peak 4 = pellotine, peak 5 = anhalonidine, peak 6 = anhalamine.

content of the "old mescal buttons" was found to be much lower than that of the "new mescal buttons". Only minor discrepancies could be observed regarding the other alkaloids (Fig. 11). It is not possible to say whether the relatively lower amount of mescaline in the old material is due to degradation of mescaline with time, or is just a natural variation.

Two compounds present in the "new mescal buttons", hordenine and 3-hydroxy-4,5-dimethoxy-phenethylamine, are almost completely lacking from the Rusby material as shown by tlc and gc (Fig. 12). These phenolic amines have apparently disappeared with time, whereas the other alkaloids of the phenolic fraction, i.e., the tetrahydroisoquinolines, are obviously more stable.

That 3-hydroxy-4,5-dimethoxyphenethylamine is present in *Lophophora williamsii* was first shown by Agurell and Lundström (1968), who found this amine to constitute about 5% of the alkaloid fraction of fresh cactus extracts. As discussed by Späth (1922), who worked with dried plant material, and later by Lundström and Agurell (1971), 3-hydroxy-4,5-dimethoxyphenethylamine is rather unstable and is quickly destroyed when alkaloid extracts are stored for a longer period of time.

II. Alkaloid patterns of Lophophora

During his field studies of *Lophophora*, Anderson (1969) also collected material for chemical study. This material was collected in Coahuila, in San Luís Potosí, and in Querétaro, and analyzed by Todd (1969). Todd used thin-layer chromatography to compare the alkaloid content of these three peyote populations, as well as of their tops and roots.

Todd found that the Querétaro material (i.e., the southern population) had a distinctly different chemical composition from that of the other two populations, which contained the same alkaloids in comparable amounts. The divergence of the Querétaro material can not be attributed to seasonal variation, as the samples were all collected in the same month (Todd, 1969).

The Querétaro material was reported to contain large amounts of pellotine, small amount of anhalamine and lophophorine, and traces only of mescaline and anhalonidine (Todd, 1969). In contrast, the percentages of the main alkaloids of *Lophophora williamsii* are as follows: mescaline 30%, pellotine 17%, anhalonidine 14%, anhalamine 8%, hordenine 8%, and lophophorine 5% of the alkaloid fraction (Lundström, 1971a). Todd interpreted his results as supporting the designation of the southern population as a distinct species, *Lophophora diffusa*, and so did Boke and Anderson (1970).

Using gas chromatography, we have now studied whole plants of *L. diffusa*, collected in Querétaro by us and found them to be richer in alkaloids than whole plants of *L. williamsii*[14] (Table I). Also, *Lophophora diffusa* produces predominantly phenolic alkaloids (98%).

From the phenolic alkaloid fraction we have isolated the major alkaloid (over 90%) and identified it as pellotine. The phenolic fraction also contained small amounts of anhalidine and trace amounts of anhalonidine and hordenine, as evident from tlc and gc (Fig. 13).

In the non-phenolic fraction (constituting only 2% of the total alkaloids) we identified trace amounts of *N*-methylmescaline by gc-ms (Fig. 14). The major part of the non-phenolic alkaloids appears to be a mixture of tetrahydroisoquinolines. The low amount of non-phenolic alkaloids in *L. diffusa* has so far prevented us from identifying these compounds.[15]

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[14]Concerning *L. williamsii* we were able to confirm Todd's finding that hordenine is almost exclusively located to the roots. The other alkaloids seem to be more evenly distributed between top and root, although the tops are much richer in alkaloids (Table I).

[15] After the completion of this manuscript, one of the minor non-phenolic tetrahydroisoquinoline alkaloids of *L. diffusa* has been identified as *O*-methylpellotine (Bruhn and Agurell, *Phytochemistry*, in press).

Fig. 13. Gas chromatographic comparison of alkaloid fractions from *Lophophora* species. 5% XE-60 on Gas Chrom P. Upper panel: Phenolic alkaloid fraction from *Lophophora diffusa*. Lower panel: Phenolic alkaloid fraction from tops of *Lophophora williamsii*.

Peak 1 = hordenine, peak 2 = pellotine, peak 3 = anhalonidine, peak 4 = anhalamine.

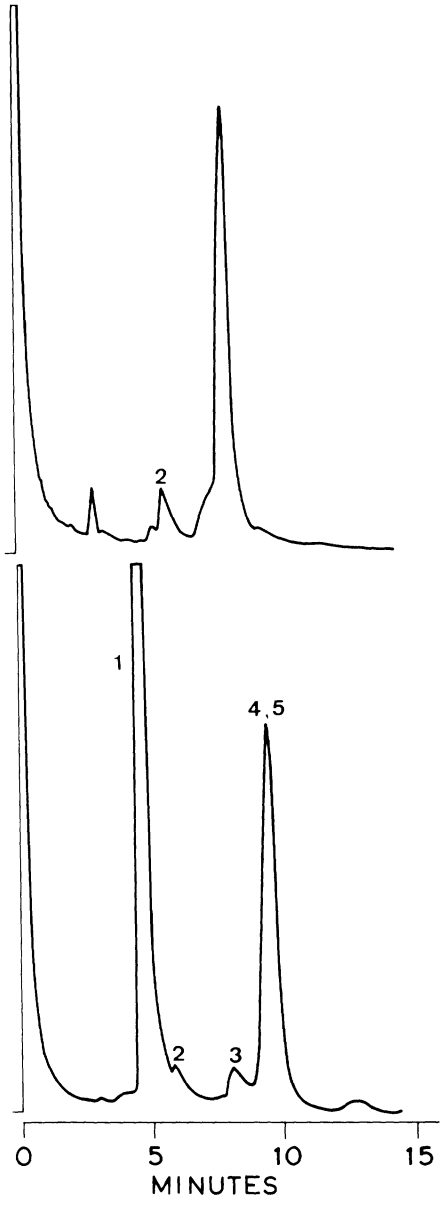

Fig. 14. Gas chromatographic comparison of alkaloid fractions from *Lophophora* species. 5% SE-30 on Gas Chrom P. Upper panel: Non-phenolic alkaloid fraction of *Lophophora diffusa*. Lower panel: Non-phenolic alkaloid fraction from tops of *Lophophora williamsii*.

Peak 1 = mescaline, peak 2 = *N*-methylmescaline, peak 3 = anhalinine, peak 4 = anhalonine, peak 5 = lophophorine.

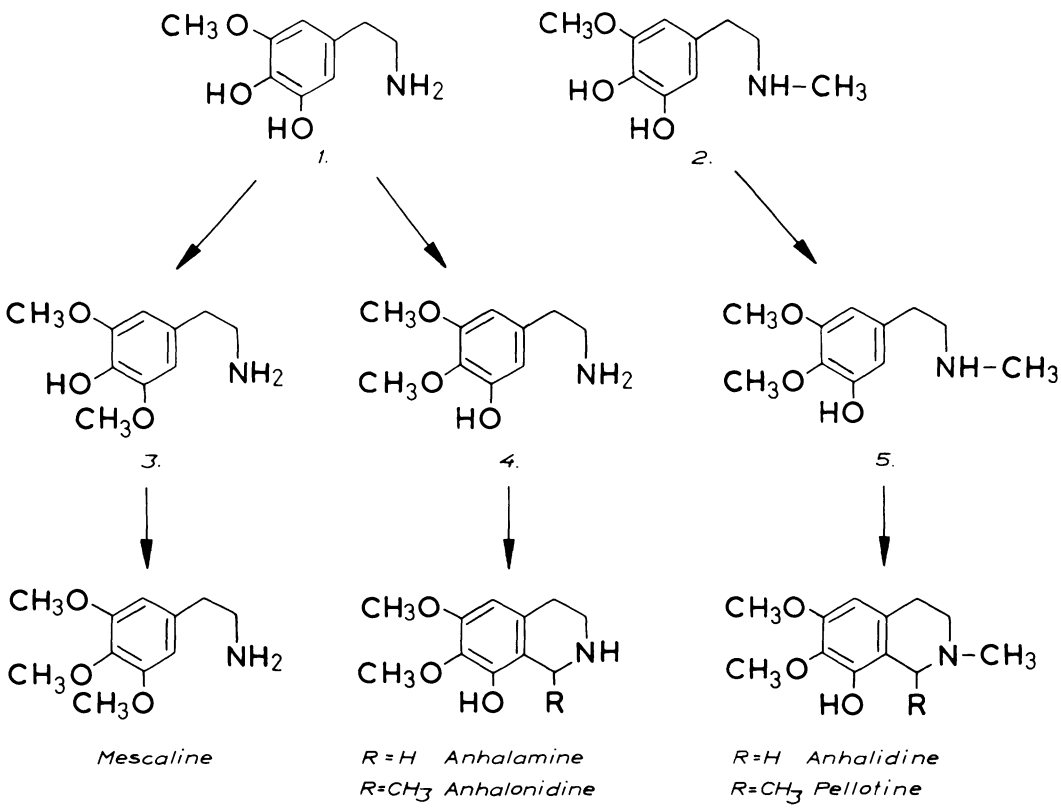

Fig. 15. Formation of mescaline and tetrahydroisoquinoline alkaloids. A discussion of the various pathways is given in the text.

When these results are compared with Todd's (1969), which were based only on tlc, some minor discrepancies can be observed. Mescaline and anhalamine can so far not be detected in our extract, and may thus be present in trace amounts only. Instead, we could identify the corresponding *N*-methylated compounds, *N*-methylmescaline and anhalidine.

In this connection, it is interesting to note that Lundström (1971a) has observed a variation of the alkaloid content of *Lophophora williamsii* following the seasons of the year. When plants were harvested in late autumn or winter, they yielded higher percentages of anhalamine and anhalonidine than of the corresponding *N*-methylated alkaloids anhalidine and pellotine. The present results with *L. diffusa* can, however, hardly be seen in support of a seasonal variation, since Todd's material was collected by Anderson, 26 June 1967, "near Vizarrón, Querétaro" (Todd, 1969) and our material was collected north of Vizarrón, 29 June 1971.

Pellotine[16] constitutes more than 90% of the alkaloid fraction of *Lophophora diffusa*. What then is the relationship between pellotine and mescaline, the major alkaloid of *Lophophora williamsii*?

[16]The name pellotine was given by Heffter (1894a) to the first alkaloid isolated by him from *Anhalonium williamsii* "pellote". But in Mexico "pellote" and "peyote" are pronounced in the same way. Both forms derive from the ancient Aztec word "peyotl", and Lewin (1894a) thus considered "peyotlin" to be a more correct name for the alkaloid. The name pellotine has, however, entered the literature and is now well established, although some authors have used the variant spelling "peyotine" (e.g.

The main biosynthetic route to mescaline and the tetrahydroisoquinoline alkaloids in *L. williamsii* proceeds from the amino acid tyrosine via tyramine, dopamine, and 3-methoxytyramine to 3,4-dihydroxy-5-methoxyphenethylamine (Kapadia and Fayez, 1970; Lundström, 1971a). This compound (*1*, Fig. 15) is an important intermediate. Methylation on the *meta* hydroxy group will give *3* and when further methylated, mescaline. *Para*-methylation of *1* yields *4*, which is favorably *ortho*-activated for ring closure to the tetrahydroisoquinoline alkaloids.

This hypothesis was first put forward by Agurell and Lundström (1968) as an explanation of the fact that *L. williamsii* contains both mescaline and tetrahydroisoquinolines, while the Peruvian cactus *Trichocereus pachanoi* produces almost solely mescaline (Lundström, 1970).

Biosynthetic experiments with *L. williamsii* verified these routes, but 3-hydroxy-4,5-dimethoxyphenethylamine (*4*, Fig. 15) was only very minutely converted into pellotine. A better precursor of pellotine, surprisingly, was 3,4-dihydroxy-5-methoxyphenethylamine (*1*, Fig. 15) (Khanna et al., 1970; Battersby et al., 1968).

A possible explanation was obtained when Lundström (1971b) found that *N*-methyl-3-hydroxy-4,5-dimethoxyphenethylamine (*5*, Fig. 15) was well incorporated into pellotine. This compound (*5*) was also identified in *L. williamsii.* The combined findings lead Lundström (1971b) to propose that pellotine, and probably also anhalidine, are formed in *L. williamsii* by a separate pathway involving *N*-methylated phenethylamine derivatives.

It is not as yet known at which step *N*-methylation occurs, but it would seem that there exists in *L. williamsii* a balance between the three routes (Fig. 15).

The formation of pellotine as the major alkaloid in *L. diffusa* may then reflect an efficient *N*- and *para-O*-methylation of the alkaloid precursors. The route *2* - *5*-anhalidine/pellotine (Fig. 15) is a likely pathway, but compound *2* has not been found as yet in *L. williamsii* or *L. diffusa.* Additional support for the existence of an efficient *N*-methylation in *L. diffusa* may be seen in our identification of *N*-methylmescaline and anhalidine, but not mescaline or anhalamine in this cactus.

So far, we do not know whether such variations in alkaloid content may occur also within the larger northern *Lophophora* population, i.e., *L. williamsii.* This species is, however, known to be highly variable morphologically. Interestingly, Boke and Anderson (1970) and Anderson and Stone (1971) believe *L. diffusa* to be the ancestral type of the two *Lophophora* species.

III. Ethnopharmacological and phytochemical implications of Lophophora diffusa

> It is always awkward doing business with an alias.
>
> SHERLOCK HOLMES

A question that poses itself is whether or not *Lophophora diffusa* has been studied earlier under a different name. We feel sure that this is the case and will point out here a few studies which in our opinion are referable to *L. diffusa.*

Anonymous, 1959) and, in Spanish, "peyotina" (e.g. Robles and Gómez Robleda, 1931). Notwithstanding, Kapadia et al. (1968) have given the name "peyotine" to the quarternary methyl derivative of pellotine, thus creating more confusion. Shulgin's reintroduction of Lewin's name "peyotline" for pellotine is also most unfortunate (Shulgin, 1973). Isopellotine was recently found in *L. williamsii* by Lundström (1972).

THE SOUTHERN TYPE

Young plant of Lophophora from Higuerillos, state of Queretaro, Mexico, the southern limit of the genus. Collected in 1905 by Dr. J. N. Rose. Photograph natural size. (Fig. 10.)

Fig. 16. The *Lophophora* from Querétaro. Illustration found in Safford's paper "*An Aztec Narcotic*" (1915).

In 1905, Altamirano reported on a botanical excursion to Querétaro, where he had obtained some interesting information from a native guide in Higuerillas, "un indígena llamado Nieves Sánchez. Este me refirió que el Peyote existe en esa región, sobre todo en el cerro del Angel, cerca del

Extoraz, de donde lo llevan frecuentemente para México en grandes cantidades. El administrador me dijo lo mismo y agregó que la cuota que le pagan por la extracción de este Peyote es de $0.12, por cada cargo de hombre; que cada hombre carga como 300 peyotes en unos cestos largos que hacen de varas, y que hay un individuo en Cadereyta que tiene como contrata la extracción de esta planta." ("a native called Nieves Sánchez. This man told me that the Peyote exists in this region, above all on the "cerro del Angel" close to Extoraz, from where it is often brought to Mexico (City) in large quantities. The administrator told me the same thing and added that for the extraction of this Peyote they pay him $0.12, for every man's load; and that every man carries about 300 peyote plants in some long baskets, which they make from rod, and that there is a person in Cadereyta who is contracted to extract this plant.")

In summarizing the results of this trip, Altamirano returned to the peyote: "Por último, debo mencionar que el Peyote se encuentra en Higuerillas; que traje dos especies llamadas así, pero que una es el *Anhalonium lewinii.* Hay también unos *Peyotes falsos* que designan con el nombre de Peyote de imitación. ("Finally, I should mention that the Peyote can be found at Higuerillas; that there are two species so called, but that one of them is the *Anhalonium lewinii.* There are also some *false Peyotes* which they call *Peyote* because of imitation.")[17] El distintivo que aquellos indígenas usan para designar el verdadero Peyote, es el de Peyote liso (*Anhalonium lewinii*), y *Peyote Chino.*" ("The attribute which these natives use to name the real Peyote, is Peyote liso (*Anhalonium lewinii*) and *Peyote Chino.*")[18] (Altamirano, 1905).

Altamirano's report shows that localities of *L. diffusa* were known around the turn of the century and that this plant was the object of an extensive trade. (Of the two *Lophophora* species, *L. diffusa* is the most easily accessible one from Mexico City). When we collected *L. diffusa,* we found that the plant is still called peyote and regarded as a medicinal plant. As far as we know, there is nowadays no such large-scale collection of *L. diffusa.*

Altamirano was accompanied on the above-mentioned field trip by Dr. J. N. Rose, cactus botanist and co-author of the classic work "The Cactaceae" (with N. L. Britton). A plant collected by Dr. Rose is pictured by Safford (1915) as: "Young plant of *Lophophora* from Higuerillos, state of Querétaro, Mexico, the southern limit of the genus. Collected in 1905 by Dr. J. N. Rose." (Fig. 16).

Although Safford (1915) believed that *Anhalonium lewinii* was only a form of *Lophophora williamsii,* he obviously thought that the Querétaro form (which he called "the southern type") was more remotely related to *L. williamsii:* "At first the writer was inclined to separate this form from both *L. williamsii* and *L. lewinii,* but after carefully comparing a number of specimens the three types seem to be connected by intermediate forms, and

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[17] One of the cacti from Querétaro which have been called peyote is *Strombocactus disciformis* (Schultes, 1937b). This name is still used for the cactus, as found by Dr. Hernando Sánchez-Mejorada and one of us (J. G. B.) on the same trip that yielded the now investigated material of *Lophophora diffusa. Turbinicarpus pseudomacrochele* is another species from this region which may be of interest in a peyote discussion (Bruhn and Bruhn, 1973).

[18] In the Herbario Nacional, Universidad Nacional Autónoma de México, Mexico City, one of the authors (J. G. B.) found a "peyote chino" (San Luís Potosí; Febrero 1956, Schwarts s.n.) determined as *Aztekium ritteri* Boed. (Cactaceae) by Dra Helia Bravo of the Instituto de Biología, UNAM. This species has earlier been listed as a "peyote" by Schultes (1937b).

they cannot, therefore, be specifically distinct. Indeed as they sometimes grow from the same base it would be improper even to designate them as varieties." (Safford, 1915). In view of the knowledge of *Lophophora* in 1915, this was no doubt a wise standpoint.

Diguet (1907) reported that in the state of Querétaro the peyote is called *señi*. Interestingly, the Kiowa Indians of Oklahoma also use the name *señi* for peyote (Shultes, 1937b). In 1931, Robles and Gómez Robleda published a study of the pharmacological action of pellotine. This study was performed in the Instituto de Biología, Universidad Nacional de México. The authors said in their introduction that they had started a study of the action of the various alkaloids extracted from *Lophophora williamsii*, but so far they had only been able to dispose of one, the hydrochloride of pellotine[19], isolated in the Sección de Química of the Instituto de Biología.

The cactus expert of the Instituto de Biología at this time was, and still is, Dra Helia Bravo. In the same year as the above-mentioned workers, she published a histological study of *Lophophora williamsii*, explicitly stating that the plants used by her had been collected in Querétaro (Bravo, 1931). Both studies were apparently part of the same research program on medicinal plants, and they were also presented at the same time (to the IX Congreso Médico Nacional), and printed in the same number of the *Anales del Instituto de Biología.*

It seemed very likely then that the material yielding pellotine was also from Querétaro, and indeed, in a recent letter to one of us (J.G.B.), Dra Bravo confirmed that the plant material used by Robles and Gómez Robleda was collected at the same time as her own material [20] (Bravo, 1973). The material was thus *L. diffusa*, and in view of our present chemical knowledge of this species, it is not surprising that pellotine should be the first alkaloid available to the physiologists.

Mescaline is responsible for the visual hallucinations of peyote intoxication, but there are also in some cases tactile, olfactory and auditory hallucinations. Lewin considered it important that "no single component of the plant, mescaline for instance, represents its total action. The other substances present in the anhalonium, which in part may act differently, cooperate and exercise an influence on the total results" (Lewin, 1964). Pellotine is also present in *L. williamsii* (18% of the alkaloid fraction), and the sedative action of this alkaloid is noted at levels that "might well be encountered in the total cactus" (Shulgin, 1973). However, mescaline dominates the pharmacological picture after taking "mescal buttons" derived from *L. williamsii.*

Pellotine constitutes more than 90% of the *L. diffusa* alkaloids. The pharmacological effects of this cactus should then resemble those of pellotine. Let us recall here that Heffter (1894a, 1896b) found in self-experiments that this alkaloid acts as a hypnotic and a sedative.

In his monograph "Der Meskalinrausch" (1927), Beringer reviewed earlier research on the pharmacological effects of the crude drug "mescal buttons".

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[19] "Hasta la fecha, solamente hemos podido disponer de uno, el Clorhidrato de peyotina, aislado en la Sección de Química del propio Instituto." (Robles and Gómez Robleda, 1931).

[20] ". . . el material de *Lophophora williamsii* procedente de Querétaro, ahora *L. diffusa* que sirvió de base para hacer el artículo publicado en An. Inst. Biol. Mex. 2(1): 3-14, fué el mismo con que trabajaron los doctores en medicina Clemente Robles y José Gómez Robleda después de haber sido elaborado en la Sección de Química del propio Instituto. El material fué colectado personalmente por mí personas que me acompañaron en el viaje a esa región." (Bravo, 1973).

Among the studies cited was the work by Jaensch, who experimented with the drug in eidetic subjects. Beringer reported that some of Jaensch's volunteers, instead of becoming excited and having hallucinations, grew very tired[21] after taking 1-2 g of the crude drug (Beringer, 1927). Jaensch's results were presented in September 1920 at the "86. Versammlung der Deutschen Naturforscher und Ärzte", and Beringer's reference is to the author's own abstract (Jaensch, 1920). Jaensch received his drug material from Lewin (as *Anhalonium lewinii*), but his short abstract does not mention any adverse effects.

So far we have not been able to find Jaensch's original paper, but if Beringer's citation is correct, a possible explanation of the tired volunteers could be the presence of *Lophophora diffusa* in the drug material. The amount of pellotine found by Jolly (1896a, 1896b) to produce sleep in his patients varied from 0.04 g to 0.08 g, and this amount could well be found in 1-2 g of dried *L. diffusa* (cf. Table I).

The most prominent side-effects of pellotine seem to be vertigo and nausea (Jolly, 1896b; Hutchings, 1897). According to Heffter (1898a), pellotine in a dose of 0.24 g does *not* cause hallucinations. Robles and Gómez Robleda (1931), using doses up to 0.30 g, observed disorientation in their subjects, who also reported hallucinations. Brossi et al. (1966) found pellotine to be hardly active as an anticonvulsive and tranquilizing drug in animal experiments. These authors add, however, that the presence of a hallucinogenic effect could not be excluded.

In discussing the possibility of a difference in "hallucinogenic value" between various *Lophophora* populations, one of us has said: "It would be an interesting problem, trying to verify whether *Lophophora diffusa* has been ritually employed or is regarded as inferior to the mescaline-producing northern "peyote" (Bruhn, 1973a, 1973b).

Already Lumholtz (1900) pointed out that the Huichol Indians recognize several kinds of *híkuli* (or *hicouri*), which is their name for peyote. Diguet (1907) discussed two varieties of peyote, one of which, called *Tzinouri-téhua-hicouri* by the Huichol Indians, was said to be more active and more bitter in taste than the other kind, called *Raitoumuanitarihua-hicouri*, which had less numerous mammillations.

According to Diguet (1907), Lumholtz (1900), and Furst (1972), the Huichol Indians collect their supply of peyote in a few sacred places in the state of San Luís Potosí, and there is no indication in these papers that they do any collecting in Querétaro. The above-mentioned names are obviously derived from *Tsinurita*, which is a mountain range close to Real de Catorce in the state of San Luís Potosí (Furst, 1972), and *Rhaitoumuany*, a locality between Real de Catorce and the city of San Luís Potosí (Diguet, 1907).

In the opinion of Rouhier (1927) the less active peyote is just a young form of *Lophophora williamsii* (cf. also La Barre, 1964). This is further indicated by the studies of Furst (1972), who found that "small, tender, five-ribbed ('five-pointed') plants are considered especially desirable. Being young, they are also less disagreeable to the taste".

Botanists have also found five-ribbed plants of *Lophophora williamsii*, and Croizat gave the name *L. williamsii* var. *pentagona* to this variety. Bravo (1967) and Anderson (1969) agreed, however, that five-ribbed plants are only a common juvenile form, not a definite variety. It would seem then that

[21] "Bei einzelnen V.P. jedoch trat statt Erregung grosse Müdigkeit auf." (Beringer, 1927, p. 31).

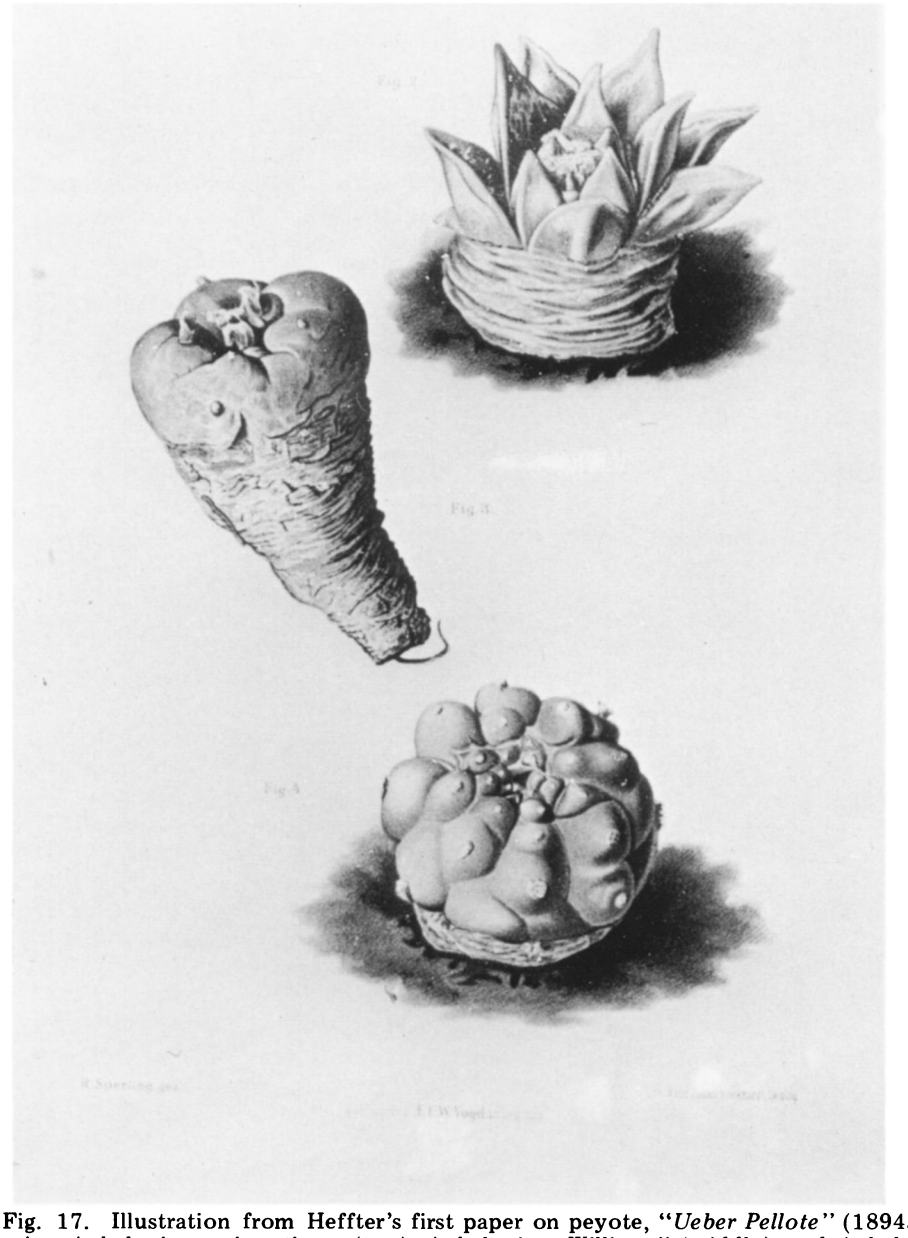

Fig. 17. Illustration from Heffter's first paper on peyote, "*Ueber Pellote*" (1894a), showing *Anhalonium prismaticum* (top), *Anhalonium Williamsii* (middle), and *Anhalonium Lewinii* (bottom), all of them drawn from living plants ("nach der Natur"). (*Anhalonium prismaticum* is now known as *Ariocarpus retusus.*)

neither the *Tzinouritéhua-hicouri* nor the *Rhaitoumuanitarihua-hicouri* can be referred to *L. diffusa.*

Let us now return to Heffter's results. He had seen more than 1600 plants of *A. lewinii* and *A. williamsii,* but he still could not distinguish the two morphologically. Chemically, however, it was easy. *A. lewinii* contained mescaline, anhalonine, anhalonidine and lophophorine, but *A. williamsii* only pellotine (Heffter, 1898a). Botanically, Schumann considered these two

species as chemical forms of the highly variable *Echinocactus williamsii* (Schumann, 1898) and concluded that these chemical forms were also *local* forms. From where, then, was Heffter's plant material obtained? *A. williamsii* was received from German cactus dealers and no collection locality was given, but the greater part of his *A. lewinii* material came directly from Saltillo in Coahuila, Mexico (Heffter, 1898a). *A. lewinii* collected in Coahuila and Texas (Parke-Davis) is no doubt referable to *Lophophora williamsii* and contains the same alkaloids.

However, in our opinion it is entirely possible that the plants of *Anhalonium williamsii*, studied by Heffter, had been collected in Querétaro and thus belonged to the concept now known as *Lophophora diffusa.* Heffter found 0.75 - 0.89% pellotine in fresh *A. williamsii* and only traces of other alkaloids (Heffter, 1896b). These results compare favorably with our present study of *L. diffusa.*[22]

An interesting observation which seems to support this view may be added here. In Anderson's key to *Lophophora*, *L. williamsii* is said to be blue-green with well-defined ribs, whereas plants of *L. diffusa* are yellow-green, usually lacking well-defined ribs (Anderson, 1969; cf. Bravo, 1967). In Heffter's first paper (1894a) there appeared a colour illustration of *A. lewinii* and *A. williamsii*, and these plants show the same differences in colour and form (Fig. 17).

In conclusion, we believe that Heffter's material of *Anhalonium williamsii*, by Schumann designated as a local chemical form, *Echinocactus williamsii* α *pellotinica*, is referable to *Lophophora diffusa* (Croizat) H. Bravo.

SUMMARY

1. The first person to draw the attention of the scientific world to peyote was doubtless Dr. J. R. Briggs, and not Mrs. A. B. Nickels as is often stated.
2. The first report of alkaloids in peyote seems to be the laboratory report by F. A. Thompson at Parke-Davis, although Louis Lewin was the first to publish.

3. The variability of *Lophophora williamsii* and imperfect knowledge of the species laid the foundation for the controversy over botanical names. Only recently have field studies in Mexico indicated that there are two species, *Lophophora williamsii* and *L. diffusa*, differing in distribution and chemical characters. *Anhalonium lewinii* is now referred to *L. williamsii.*

4. Present and earlier studies of the Querétaro peyote, *Lophophora diffusa*, show that this species differs considerably in its alkaloid set-up from *L. williamsii. L. diffusa* produces predominantly (> 90%) phenolic tetrahydroisoquinoline alkaloids (mainly pellotine) and almost no mescaline. This lends support to the earlier postulation of an independent metabolic pathway to pellotine and anhalidine.

5. In our opinion, Heffter's results with *Anhalonium williamsii* can be explained if we assume that his plant material was collected in Querétaro and was in fact *L. diffusa.* The alkaloid analysis of *L. diffusa* also provides an explanation of other controversial points in the history of peyote research.

[22] It seems especially appropriate here to recall that Kauder (p. 23) said: "The circumstances seem to me to call for further clarification, which will only be possible when we succeed in obtaining that cactus, which only contains pellotine."

6. An 80-year old sample of "mescal buttons" has been shown to still contain identifiable alkaloids, most notably mescaline.

ACKNOWLEDGMENTS

Studies on Cactaceae alkaloids were conducted by Bruhn in Mexico in 1971. We would like to thank the following persons for their hospitality and assistance: Dr. Efrén C. del Pozo, Dr. Agustín Ayala Castañares and Dr. Arturo Gómez Pompa (Universidad Nacional Autónoma de México, Mexico City). Special thanks are due to Sra. Helia Bravo Hollis and Sr. Hernando Sánchez-Mejorada (Instituto de Biología, UNAM), who helped in collecting and identifying cacti and also gave us access to their collection of Cactaceae literature.

The assistance of Catarina Bruhn in library research and in collecting and extracting *Lophophora diffusa*, and of Eva Forsén in the laboratory, is greatly appreciated. For valuable discussions we are indebted to Dr. Jan Lundström. Mass spectra were recorded by Dr. Jan-Erik Lindgren, and the manuscript was patiently typed by Miss Anna Lena Skeberg. Dr. Michael Orme kindly corrected our English.

We wish to thank Mr. G. A. Bender for permission to study his collection of early Parke-Davis correspondence. Permission to use the map of *Lophophora* distribution was kindly given by Dr. E. F. Anderson (Whitman College, Walla Walla). We also express our gratitude to Mrs. Irene Sachs (New York) for translating Hennings' letter and for allowing us to publish part of Louis Lewin's travel account, and to Mrs. Hertha Jaffé and Mr. Mordechai Yaffé (Israel) for help with the translation. Deutsche Staatsbibliothek (Berlin) furnished information on Louis Lewin, and Ms. Elizabeth Rainey of the library of the Southwestern Medical School at Dallas, University of Texas, was extremely helpful in providing documents concerning John Raleigh Briggs.

The authors are thankful to Professor Richard Evans Schultes and Dr. Stig Agurell for their encouragement and support during this work.

The research reported in this paper was supported in part (Bruhn) by the Swedish Natural Science Research Council (2451-9; 2451-10); and in part (Holmstedt) by the Swedish Medical Research Council (B74-40Y-2375-07; B74-04X-4041-02B and B74-70E-3743-02); the National Institute of Health (NIH MH12007); the Bank of Sweden Tercentenary Fund (68/53:1); the Wallenberg Foundation, and by funds from the Karolinska Institute.

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BOOK REVIEWS

The Genus Lesquerella (Cruciferae) in North America. Reed C. Rollins and Elizabeth A. Shaw. 288 pp. illus. Harvard University Press, Cambridge, Massachusetts, 1973. $18.00

Lesquerella is a genus of primarily herbaceous plants in the mustard family (Cruciferae). This book consists principally of descriptions, keys, synonymy, and comments on habitats, phenology, and nomenclature for 69 species and 29 interspecific taxa ranging from the arctic to southern Mexico. Most of the taxa are illustrated by either line drawings or photographic silhouettes. The distribution of each taxon is represented by large clear dot maps. Representative specimens examined are cited.

Biosystematists probably would have wished for more in-depth discussion and documentation on the limits of the genus, breeding systems, interspecific hybridization, chemistry, and evolutionary trends. However, cytologists will welcome the tabularized list of all known chromosome numbers and their documented sources. The discussions of pollen grains and trichomes are accompanied with clear scanning electron microscope photographs.

This book is based on more than 30 years' study of the genus by Professor Rollins. Information has been gleaned from more than 9,000 herbarium specimens, the culture of plants in the greenhouse and experimental garden, and the study of natural populations in the field. The book attempts to eliminate some of the inadequacies and deficiencies of Payson's *Monograph* of 1922, while at the same time it does not consider some of the speculative evolutionary and phylogenetic relationships believed important to Payson. The Rollins and Shaw treatment, prepared in the true classical and traditional sense, is one that would be expected as an issue or a part of a journal whose primary concern is publishing taxonomic monographs or revisions. Having a taxonomic monograph as a separate book published by a university press is a welcome, although not totally new, innovation that hopefully some other university presses will adopt.

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A Guide to Air Quality Monitoring with Lichens. William C. Denison. 39 pp. illus. Lichen Technology, Inc., Corvallis, Oregon, 1973. $3.00

A better title for this work might be *A guide to selected lichen sampling on* Quercus garryana *in the Willamette Valley, Oregon*. Based on a class project by several students, and available from the publisher at P. O. Box 369, Corvallis, Oregon 97330, it is apparently intended to serve as a base-line study on local lichen sampling that could be repeated by untrained persons in nearby areas. The publication features accurate and instructive drawings and descriptions of external structure of some 20 corticolous lichens common in the region. Forms for compiling data are provided, together with a 5-point scale of air purity based on presence and luxuriance of certain of the 20 indicator species. The work accomplishes its aim of presenting a simplified method to use lichens as pollution indicators at the local level in the Corvallis area. The oversimplification, however, is a matter for concern. The likelihood of a beginner identifying *Rinodina marysvillensis* or *Lecanora carpinea* based on these drawings and descriptions is remote, particularly when the reader is not warned about the dozens of similar crustose taxa on the same substrate or about microscopic characteristics such as spore morphology that are diagnostic to separate crustose

Book Reviews *(continued on page 413)*